

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Wikberg *et al.*

Application No. *To be assigned*;
(Continuation of U.S. Appl. No. 08/387,805,
§ 371 Date: February 21, 1995)

Filed: *Herewith*

For: **Human Melanocyte Stimulating
Hormone Receptor Polypeptide and
DNA (as amended)**

Art Unit: *To Be Assigned*

Examiner: *To Be Assigned*

Atty. Docket: 1808.0010002/MAC/MBT

Preliminary Amendment

Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicants submit the following Amendment and Remarks. This Amendment is provided in the following format:

(A) A clean version of each replacement paragraph/section/claim along with clear instructions for entry; and

(B) Starting on a separate page, a marked-up version entitled: "Version with markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Title:

Please delete the title and add the following title:

--Human Melanocyte Stimulating Hormone Receptor Polypeptide and DNA--

In the Specification:

Please add the following paragraph beginning on page 1, line 2:

--Cross Reference to Related Applications

This application is a continuation of U.S. Patent Application No. 08/387, 805, § 371 Date, February 21, 1995, which is a U.S. National Phase of PCT/DK93/00273 International Application, filed August 20, 1993; which claims priority to DK 1046/92, filed August 21, 1992; DK 1118/92, filed September 10, 1992; and DK 0528/93, filed May 5, 1993.--

Please delete the Sequence Listing that is now on specification pages 95-109, and insert the attached Sequence Listing therein.

In the Claims:

Please cancel claims 2-53 without prejudice or disclaimer.

Please add the following claims:

54. (New) A purified DNA comprising a nucleotide sequence selected from the group consisting of

- (a) a nucleotide sequence that
 - (i) hybridizes to the complement of the DNA sequence set forth in base nos. 616-1590 of SEQ ID No. 15, and
 - (ii) remains hybridized to the complement of the DNA sequence of base nos. 616-1590 of SEQ ID No. 15 when subjected to a solution of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes;
 - (b) a nucleotide sequence that is at least 95% homologous to the nucleotide sequence encoding the melanocyte stimulating hormone receptor amino acid sequence encoded by the genomic clone contained in Deutsche Sammlung von Mikroorganismen Deposit No. DSM 8440; and
 - (c) a nucleotide sequence that is at least 95% homologous to the DNA sequence set forth in base nos. 616-1590 of SEQ ID No. 15.
55. (New) The purified DNA of claim 54, wherein said nucleotide sequence
- (a) hybridizes to the complement of the DNA sequence set forth in base nos. 616-1590 of SEQ ID No. 15; and
 - (b) remains hybridized to the complement of the DNA sequence of base nos. 616-1590 of SEQ ID No. 15 when subjected to a solution of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes.
56. (New) The purified DNA of claim 54, wherein said nucleotide sequence is at least 95% homologous to the nucleotide sequence encoding the melanocyte

stimulating hormone receptor amino acid sequence encoded by the genomic clone contained in Deutsche Sammlung von Mikroorganismen Deposit No. DSM 8440.

57. (New) The purified DNA of claim 54; wherein said nucleotide sequence is at least 95% homologous to the DNA sequence set forth in base nos. 616-1590 of SEQ ID No. 15.
58. (New) A vector comprising a nucleotide sequence selected from the group consisting of
- (a) a nucleotide sequence that
 - (i) hybridizes to the complement of the DNA sequence set forth in base nos. 616-1590 of SEQ ID No. 15, and
 - (ii) remains hybridized to the complement of the DNA sequence of base nos. 616-1590 of SEQ ID No. 15 when subjected to a solution of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes;
 - (b) a nucleotide sequence that is at least 95% homologous to the nucleotide sequence encoding the melanocyte stimulating hormone receptor amino acid sequence encoded by the genomic clone contained in Deutsche Sammlung von Mikroorganismen Deposit No. DSM 8440; and
 - (c) a nucleotide sequence that is at least 95% homologous to the DNA sequence set forth in base nos. 616-1590 of SEQ ID No. 15.

59. (New) The vector of claim 58, wherein said nucleotide sequence
- (a) hybridizes to the complement of the DNA sequence set forth in base nos. 616-1590 of SEQ ID No. 15; and
 - (b) remains hybridized to the complement of the DNA sequence of base nos. 616-1590 of SEQ ID No. 15 when subjected to a solution of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes.
60. (New) The vector of claim 58, wherein said nucleotide sequence is at least 95% homologous to the nucleotide sequence encoding the melanocyte stimulating hormone receptor amino acid sequence encoded by the genomic clone contained in Deutsche Sammlung von Mikroorganismen Deposit No. DSM 8440.
61. (New) The vector of claim 58, wherein said nucleotide sequence is at least 95% homologous to the DNA sequence set forth in base nos. 616-1590 of SEQ ID No. 15.
62. (New) A host cell comprising the vector of claim 59.
63. (New) A host cell comprising the vector of claim 60.
64. (New) A host cell comprising the vector of claim 61.

65. (New) A method of making the host cell of claim 62, said method comprising transforming or transfecting a host cell with said vector.
66. (New) A method of making the host cell of claim 63, said method comprising transforming or transfecting a host cell with said vector.
67. (New) A method of making the host cell of claim 64, said method comprising transforming or transfecting a host cell with said vector.
68. (New) A method of making a vector, said method comprising inserting into a vector a nucleotide sequence selected from the group consisting of
- (a) a nucleotide sequence encoding the amino acid sequence of amino acids 1-325 of SEQ ID NO: 16;
 - (b) the DNA sequence set forth in base nos. 616-1590 of SEQ ID No. 15;
 - (c) a nucleotide sequence that
 - (i) hybridizes to the complement of the DNA sequence set forth in base nos. 616-1590 of SEQ ID No. 15, and
 - (ii) remains hybridized to the complement of the DNA sequence of base nos. 616-1590 of SEQ ID No. 15 when subjected to a solution of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes;

- (d) a nucleotide sequence encoding the melanocyte stimulating hormone receptor amino acid sequence encoded by the genomic clone contained in Deutsche Sammlung von Mikroorganismen Deposit No. DSM 8440;
 - (e) the genomic clone contained in Deutsche Sammlung von Mikroorganismen Deposit No. DSM 8440; and
 - (f) a nucleotide sequence that is at least 95% homologous to the nucleotide sequence of (a), (b) (d) or (e).
69. (New) The method of claim 68, wherein said nucleotide sequence
- (a) hybridizes to the complement of the DNA sequence set forth in base nos. 616-1590 of SEQ ID No. 15; and
 - (b) remains hybridized to the complement of the DNA sequence of base nos. 616-1590 of SEQ ID No. 15 when subjected to a solution of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes.
70. (New) The method of claim 68, wherein said nucleotide sequence encodes the melanocyte stimulating hormone receptor amino acid sequence encoded by the genomic clone contained in Deutsche Sammlung von Mikroorganismen Deposit No. DSM 8440.

71. (New) The method of claim 68, wherein said nucleotide sequence is the genomic clone contained in Deutsche Sammlung von Mikroorganismen Deposit No. DSM 8440.
72. (New) The method of claim 68, wherein said nucleotide sequence is at least 95% homologous to the nucleotide sequence of (a), (b) (d) or (e).
73. (New) A method of making a vector, said method comprising inserting into a vector a nucleotide sequence encoding the amino acid sequence of amino acids 1-325 of SEQ ID No. 16.
74. (New) The method of claim 73, wherein said nucleotide sequence is the DNA sequence set forth in base nos 616-1590 of SEQ ID No. 15.
75. (New) A purified DNA comprising a nucleotide sequence that is at least 95% homologous to base nos. 1-306 of SEQ ID No. 7.
76. (New) A vector comprising the nucleotide sequence of claim 75.
77. (New) A method of making a vector, said method comprising inserting into a vector a nucleotide sequence that is at least 95% homologous to base nos. 1-306 of SEQ ID No. 7.

78. (New) A host cell comprising the vector of claim 76.
78. (New) A method of making the host cell of claim 78, comprising transforming or transfecting a host cell with said vector.
79. (New) A purified DNA comprising a nucleotide sequence that is at least 95% homologous to base nos. 1-312 of SEQ ID No. 9.
81. (New) A vector comprising the nucleotide sequence of claim 80.
82. (New) A method of making a vector, said method comprising inserting into a vector a nucleotide sequence that is at least 95% homologous to base nos. 1-312 of SEQ ID No. 9.
83. (New) A host cell comprising the vector of claim 81.
84. (New) A method of making the host cell of claim 83, comprising transforming or transfecting a host cell with said vector.
85. (New) A purified DNA comprising a nucleotide sequence comprising base nos. 1-1270 of SEQ ID No. 1.

86. (New) A vector comprising a nucleotide sequence comprising base nos. 1-1270 of SEQ ID No. 1.
87. (New) A method of making a vector comprising inserting into a vector a nucleotide sequence comprising base nos. 1-1270 of SEQ ID No 1.
88. (New) A host cell comprising the vector of claim 86.
88. (New) A method of making the host cell of claim 88, comprising transforming or transfecting a host cell with said vector.
90. (New) The host cell obtained by the method of claim 89.
91. (New) A purified DNA comprising a nucleotide sequence comprising base nos. 1-285 of SEQ ID No. 5.
92. (New) A vector comprising the nucleotide sequence of claim 91.
93. (New) A method of making a vector comprising inserting into a vector a nucleotide sequence comprising base nos. 1-285 of SEQ ID No. 5.
94. (New) A host cell comprising the vector of claim 92.

95. (New) A method of making the host cell of claim 94, comprising transforming or transfecting a host cell with said vector.
96. (New) A purified polypeptide comprising a polypeptide having an amino acid sequence of amino acids 1-95 of SEQ ID No. 6.
97. (New) A purified DNA comprising a nucleotide sequence selected from the group consisting of
 - (a) a nucleotide sequence encoding the amino acid sequence set forth in SEQ ID NO: 8;
 - (b) a nucleotide sequence that hybridizes to the complement of SEQ ID NO: 7 and remains hybridized under the wash conditions of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes; and
 - (c) a nucleotide sequence that is at least 95% homologous to the nucleotide sequence of (a).
98. (New) The purified DNA of claim 97, wherein said nucleotide sequence encodes the amino acid sequence set forth in SEQ ID NO: 8.
99. (New) The purified DNA of claim 97 wherein said nucleotide sequence is selected from the group consisting of:

- (a) a nucleotide sequence that hybridizes to the complement of SEQ ID NO: 7 and remains hybridized under the wash conditions of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes; and
- (b) a nucleotide sequence that is at least 95% homologous to the nucleotide sequence encoding SEQ ID NO: 8.

100. (New) A vector comprising the purified DNA of claim 97.

101. (New) A vector comprising the purified DNA of claim 98.

102. (New) A vector comprising the purified DNA of claim 99.

103. (New) A purified DNA comprising a nucleotide sequence selected from the group consisting of

- (a) a nucleotide sequence encoding the amino acid sequence set forth in SEQ ID NO: 10;
- (b) a nucleotide sequence that hybridizes to the complement of SEQ ID NO: 9 and remains hybridized under the wash conditions of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes; and
- (c) a nucleotide sequence that is at least 95% homologous to the nucleotide sequence of (a).

104. (New) The purified DNA of claim 103, wherein said nucleotide sequence encodes the amino acid sequence set forth in SEQ ID NO: 10.
105. (New) The purified DNA of claim 103 wherein said nucleotide sequence is selected from the group consisting of
- (a) a nucleotide sequence that hybridizes to the complement of SEQ ID NO: 9 and remains hybridized under the wash conditions of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes; and
 - (b) a nucleotide sequence that is at least 95% homologous to a nucleotide sequence encoding SEQ ID NO: 10.
106. (New) A vector comprising the purified DNA of claim 103.
107. (New) A vector comprising the purified DNA of claim 104.
108. (New) A vector comprising the purified DNA of claim 105.
109. (New) The vector of claim 106, wherein the vector is an expression vector.
110. (New) A host cell comprising the vector of claim 109.

111. (New) The host cell of claim 110, wherein said host cell is capable of replicating said vector.
112. (New) The host cell of claim 111, wherein said nucleotide sequence is integrated into the genome of said host cell.
113. (New) A composition comprising the host cell of claim 112, wherein said host cell is disrupted.
114. (New) A method of making a host cell comprising transforming or transfecting a host cell with the vector of claim 106.
115. (New) A host cell comprising the vector of claim 107.
116. (New) A host cell comprising the vector of claim 108.
117. (New) A purified polypeptide comprising a polypeptide sequence that is at least 95% homologous to amino acids 1-102 of SEQ ID No. 8.
118. (New) A purified polypeptide comprising an amino acid sequence selected from the group consisting of
 - (a) the amino acid sequence set forth in SEQ ID NO: 8;

- (b) an amino acid sequence encoded by a nucleotide sequence that hybridizes to the complement of SEQ ID NO: 7 and remains hybridized under the wash conditions of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes; and
- (c) the purified polypeptide of claim 64, wherein said polypeptide further contains at least one modification selected from the group consisting of glycosylation, coupling to a carbohydrate or lipid moiety, the presence of a palmitoyl anchor or part thereof, detectable labeling, and to a solid support.

- 119. (New) The purified polypeptide of claim 118, said polypeptide being in substantially pure form.
- 120. (New) The purified polypeptide of claim 118, said polypeptide being in lipid-soluble form.
- 121. (New) A fusion polypeptide comprising a first polypeptide fused to a second polypeptide, wherein said first polypeptide comprises the polypeptide of claim 118.
- 122. (New) The purified polypeptide of claim 118, wherein said polypeptide encodes a melanocyte stimulating hormone receptor that exhibits a K_i for NDP-MSH of less than 10 nM in a NDP-MSH binding assay.

123. (New) A purified polypeptide comprising a polypeptide sequence that is at least 95% homologous to amino acids 1-104 of SEQ ID No. 10.
124. (New) A purified polypeptide comprising an amino acid sequence selected from the group consisting of
- (a) the amino acid sequence set forth in SEQ ID NO: 10;
 - (b) an amino acid sequence encoded by a nucleotide sequence that hybridizes to the complement of SEQ ID NO: 9 and remains hybridized under the wash conditions of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes; and
 - (c) the purified polypeptide of claim 70, wherein said polypeptide further contains at least one modification selected from the group consisting of glycosylation, coupling to a carbohydrate or lipid moiety, the presence of a palmitoyl anchor or part thereof, detectable labeling, and to a solid support.
125. (New) The purified polypeptide of claim 124, said polypeptide being in substantially pure form.
126. (New) The purified polypeptide of claim 124, said polypeptide being in lipid-soluble form.

127. (New) A fusion polypeptide comprising a first polypeptide fused to a second polypeptide, wherein said first polypeptide comprises the polypeptide of claim 124.
128. (New) The purified polypeptide of claim 124, wherein said polypeptide encodes a melanocyte stimulating hormone receptor that exhibits a K_d for NDP-MSH of less than 10 nM in a NDP-MSH binding assay.
129. (New) A purified polypeptide comprising a polypeptide sequence that is at least 95% homologous to amino acids 1-325 of SEQ ID NO: 16.
130. (New) A purified polypeptide comprising an amino acid sequence selected from the group consisting of
- (a) the amino acid sequence set forth in SEQ ID NO: 16;
 - (b) an amino acid sequence encoded by a nucleotide sequence that hybridizes to the complement of SEQ ID NO: 15 and remains hybridized under the wash conditions of 0.1X SSC and 0.1% SDS at 65°C for 20 minutes; and
 - (c) the purified polypeptide of claim 75, wherein said polypeptide further contains at least one modification selected from the group consisting of glycosylation, coupling to a carbohydrate or lipid moiety, the presence of a palmitoyl anchor or part thereof, detectable labeling, and to a solid support.

131. (New) The purified polypeptide of claim 130, said polypeptide being in substantially pure form.
132. (New) The purified polypeptide of claim 130, said polypeptide being in lipid-soluble form.
133. (New) A fusion polypeptide comprising a first polypeptide fused to a second polypeptide, wherein said first polypeptide comprises the polypeptide of claim 130.
134. (New) The purified polypeptide of claim 130, wherein said polypeptide encodes a melanocyte stimulating hormone receptor that exhibits a K_i for NDP-MSH of less than 10 nM in a NDP-MSH binding assay.
135. (New) A purified polypeptide comprising a polypeptide having an amino acid sequence selected from the group consisting of
- (a) amino acids 1-317 of SEQ ID No. 2; and
 - (b) the amino acid sequence of the melanocyte stimulating hormone receptor amino acid sequence encoded by the cDNA clone contained in Deutsche Sammlung von Mikroorganismen Deposit No. DSM 7214.

136. (New) The purified polypeptide of claim 135, wherein said polypeptide comprises a polypeptide having an amino acid sequence of amino acids 1-317 of SEQ ID No. 2.
137. (New) The purified polypeptide of claim 135, wherein said polypeptide comprises a polypeptide having the amino acid sequence of the melanocyte stimulating hormone receptor amino acid sequence encoded by the cDNA clone contained in Deutsche Sammlung von Mikroorganismen Deposit No. DSM 7214.
138. (New) The purified polypeptide of claim 136, wherein said polypeptide encodes a melanocyte stimulating hormone receptor that exhibits a K_i for NDP-MSH of less than 10 nM in a NDP-MSH binding assay.
139. (New) The purified polypeptide of claim 137, wherein said polypeptide encodes a melanocyte stimulating hormone receptor that exhibits a K_i for NDP-MSH of less than 10 nM in a NDP-MSH binding assay.

Remarks

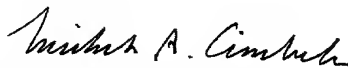
Upon entry of the foregoing amendment, claims 1 and 54-139 are pending in the application, with claims 1, 54, 58, 68, 73, 75, 77, 80, 82, 85, 86, 87, 91, 93, 96, 97, 103, 117, 118, 123, 124, 129, 130 and 135 being the independent claims. Claims 2-53 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 54-139 are sought to be added. Support for new claims 54-139 is found, *inter alia*, in original claims 2-53. Support is additionally found for the nucleic acid ranges of claims 54-74 in the specification on page 12, lines 11-13, and page 37, lines 3-12; for the DSM 7214 and 8440 deposits in original claim 26; the hybridization and wash conditions on page 7, lines 18-20; and the NDP-MSH binding assay on pages 49 and 82 of the specification, Example 3 and Figures 5, 6 and 9; and, elsewhere throughout the specification. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Conclusion

It is respectfully believed that the present application is in condition for examination. Early notice to this effect is earnestly solicited. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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Version with markings to show changes made

In the title:

The title was deleted and the following title was substituted therefor:

"Human Melanocyte Stimulating Hormone Receptor Polypeptide and DNA"

Claims 2-53 were cancelled without prejudice.

New claims 54-139 were added.